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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

J. YUN TSO

Application No.: 09/618,380

Filed: July 17, 2000

For: BISPECIFIC ANTIBODY
EFFECTIVE TO TREAT B-CELL
LYMPHOMA AND CELL LINE

Art Unit: 1642

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Prior to examination of the above-referenced application, please enter the following amendments and remarks.

IN THE CLAIMS:

Please cancel claims 16-18 without prejudice.

Please add the following new claims.

B1 1/24/01 A humanized antibody comprising a humanized heavy chain and humanized light chain, wherein:

(1) the humanized heavy chain variable region comprises three complementarity determining regions (CDRs) from the mouse M291 heavy chain and a framework from a human acceptor antibody heavy chain, optionally having one or more human framework residues that interact with one of the CDRs substituted with mouse framework residues from corresponding positions in the M291 heavy chain variable region framework, and

62

B

(2) the humanized light chain variable region comprises three complementarity determining regions from the mouse M291 light chain and a framework from a human acceptor antibody light chain optionally having one or more human framework residues that interact with one of the CDRs substituted with mouse framework residues from corresponding positions in the M291 light chain variable region framework; and

the humanized antibody specifically binds to a CD3 antigen on the surface of T cells, wherein the mouse M291 antibody has a heavy chain with a variable region of sequence SEQ. ID. No. 11 and a light chain with a variable region of sequence SEQ. ID. No. 9.

B1
cont.
2352
The antibody of claim *24* which binds to a CD3 antigen on the surface of T cells with a binding affinity of at least $10^7 M^{-1}$.

3383
The antibody of claim *25* which binds to a CD3 antigen on the surface of T cells with a binding affinity of at least $10^8 M^{-1}$.

4374
The antibody of claim *24* which is of the IgG1 isotype.

5385
The antibody of any one of claims *24*, *25* or *26* wherein at least one of the light chain human framework residues that interact with one of the CDRs is substituted with a mouse amino acid from the corresponding position in the M291 light chain variable region framework.

6386
The antibody of any one of claims *24*, *25* or *26* wherein at least one of the heavy chain human framework residues that interact with one of the CDRs is substituted with a mouse amino acid from the corresponding position in the M291 heavy chain variable region framework.

Sub D2
40. The antibody of claim 39 wherein said position is selected from the group H30, H67, H68, H70, H72 and H74.

Sub D3
41. A humanized antibody that specifically binds to a CD3 antigen on the surface of T cells, comprising a pair of humanized heavy chains and humanized light chains, wherein the humanized light chain variable region comprises the amino acid sequence of Fig. 5A (upper lines) (SEQ. ID. No. 8) and the humanized heavy chain variable region comprises the amino acid sequence of Fig. 5B (SEQ. ID. No. 10)

D1
--The present application is a continuation of 08/397,411, filed March 1, 1995, now US 6,129,914, which is a continuation-in-part of 07/859,583, filed March 27, 1992, ^{1 NOW ADD.} all incorporated by reference.--

In the claims

Please amend claim 40 as follows:

D2
~~740~~ ~~740~~ ⁶ ~~396~~ (Amended) The antibody of claim ~~39~~ wherein said position is selected from the group consisting of H30, H67, H68, H70, H72 and H74.

Please amend claim 41 as follows:

D3
~~8418~~ (Amended) A humanized antibody that specifically binds to a CD3 antigen on the surface of T cells, comprising a pair of humanized heavy chains and humanized light chains, wherein the humanized light chain variable region comprises the amino acid sequence of Fig. 5A (upper lines) (SEQ. ID. No. 8) and the humanized heavy chain variable region comprises the amino acid sequence of Fig. 5B (upper lines) (SEQ. ID. No. 10).

Please cancel claim 42.

Please add the following new claim:

D4
~~9439~~ A bispecific antibody comprising;
a first Fab' fragment comprising the humanized heavy chain variable region comprises the amino acid sequence of Fig. 5B (upper lines) (SEQ. ID. No. 10) and the humanized light chain variable region comprises the amino acid sequence of Fig. 5A (upper lines) (SEQ. ID. No. 8),